

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 640100-352	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 99/ 27129	International filing date (<i>day month year</i>) 16/11/1999	(Earliest) Priority Date (<i>day month year</i>) 16/11/1998
Applicant OSIRIS THERAPEUTICS, INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US 99/27129

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons

- 1 ☒ Claims Nos. -
because they relate to subject matter not required to be searched by this Authority, namely
Although claims 9-11 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
- 2 ☐ Claims Nos. -
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
- 3 ☐ Claims Nos. -
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

- 1 ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
- 2 ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
- 3 ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos. -
- 4 ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims, it is covered by claims Nos. -

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest
- ☐ No protest accompanied the payment of additional search fees

PATENT COOPERATION TREATY

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REC'D 27 JUL 2001

INTERNATIONAL PRELIMINARY EXAMINATION REPORT PCT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 640100-352	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/27129	International filing date (day/month/year) 16 NOVEMBER 1999	Priority date (day/month/year) 16 NOVEMBER 1998
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant OSIRIS THERAPEUTICS, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 15 JUNE 2000	Date of completion of this report 18 JUNE 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer <i>David M. Naff</i> DAVID M. NAFF
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/27129

I. Basis of the report

1. With regard to the **elements** of the international application:*

- ☒ the international application as originally filed
- ☒ the description:
pages 1-16, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____
- ☒ the claims:
pages 17-18, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____
- ☒ the drawings:
pages 1-9, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____
- ☒ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/fig. NONE

5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/27129

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims <u>2, 3, 5, 8</u>	YES
	Claims <u>1, 4, 6, 7, 9-11</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-11</u>	NO
Industrial Applicability (IA)	Claims <u>1-11</u>	YES
	Claims <u>NONE</u>	NO

2. citations and explanations (Rule 70.7)

Claims 1, 4, 6, 7 and 9-11 lack novelty under PCT Article 33(2) as being anticipated by Reprogenesis, Inc. (WO 98/25653) or Morphogen Pharmaceuticals, Inc. (WO 96/28539).

Reprogenesis, Inc. or Morphogen Pharmaceuticals, Inc. disclose generating cartilage in vivo by forming an alginate gel containing human mesenchymal stem cells and implanting the gel. Alternatively, an alginate solution containing the cells is formed, the solution injected where cartilage is to be generated, and the alginate is gelled.

Claims 2, 3, 5 and 8 lack an inventive step under PCT Article 33(3) as being obvious over Reprogenesis, Inc. or Morphogen Pharmaceuticals, Inc. in view of Osiris Therapeutics, Inc. (WO 98/32333).

Osiris Therapeutics, Inc. discloses using a chondroinductive agent to induce differentiation of mesenchymal stem cells into chondrocytes. The agent can be a component of collagenous extracellular matrix (page 12, line 11 of second full paragraph) which can be hyaluronic acid (page 15, line 8 of first full paragraph).

It would have been obvious to combine the stem cells of Reprogenesis, Inc. or Morphogen Pharmaceuticals, Inc. with a component of extracellular matrix such as hyaluronic acid to obtain its chondroinductive function to induce differentiation of mesenchymal stem cells into chondrocytes as suggested by Osiris Therapeutics, Inc.

Claims 2, 3, 5 and 8 meet the criteria set out in PCT Article 33(2) because a single document does not disclose or suggest the claimed invention.

Claims 2, 3, 5 and 8 meet the criteria set out in PCT Article 33(4) because the claimed invention has utility and therefore has industrial applicability.

(Continued on Supplemental Sheet.)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/27129

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): A01N 63/00; C12N 11/10, 5/00, 5/06, 5/08 and US Cl.: 424/93.7, 423; 435/178, 366, 377, 382, 395, 387

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):

_____ NEW CITATIONS _____

NONE

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

To:

Carella, Byrne, Bain, Gilfillan,
Cecchi, Stewart & Olstein
Attn. OLSTEIN, Elliot M.
6 Becker Farm Road
Roseland, New Jersey 07068
UNITED STATES OF AMERICA

Date of mailing
(day/month/year)

26/04/2000

Applicant's or agent's file reference

640100-352

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/US 99/ 27129

International filing date

(day/month/year)

16/11/1999

Applicant

OSIRIS THERAPEUTICS, INC. et al.

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Véronique Baillou

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

INTERNATIONAL SEARCH REPORT

International Application No.

T/US 99/27129

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C12N5/06 A61K35/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 25653 A (ATALA ANTHONY ; NELSON GORDON P (US); ZHOU TAO (US); BORLAND KERMIT) 18 June 1998 (1998-06-18)	1, 4, 6, 7, 9-11
Y	page 3, line 5 -page 3, line 16 page 18, line 22 -page 27, line 19 page 30, line 27 -page 33, line 3 ---	2, 3, 5, 8
X	WO 96 28539 A (MORPHOGEN PHARMACEUTICALS INC ; NORTH SHORE UNIVERSITY HOSPITAL (US)) 19 September 1996 (1996-09-19)	1, 4, 6, 7, 9-11
Y	page 6, line 11 -page 6, line 17 page 11, line 8 -page 11, line 17 --- -/--	2, 3, 5, 8

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

Special categories of cited documents

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

5 April 2000

Date of mailing of the international search report

26. 04. 00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel (+31-70) 340-2040, Tx 31 651 epo.nl,
 Fax (+31-70) 340-3016

Authorized officer

Morawetz, R

INTERNATIONAL SEARCH REPORT

International Application No

T/US 99/27129

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	SHAKIBAEI, M. AND P. DE SOUZA : "Differentiation of mesenchymal limb bud cells to chondrocytes in alginate beads" CELL BIOLOGY INTERNATIONAL, vol. 21, no. 2, 1997, pages 75-86, XP000881943 cited in the application	1,4,6
Y	page 75, right-hand column, paragraph 2 -page 76, left-hand column, paragraph 2 page 81, left-hand column, paragraph 1 -page 84, right-hand column, paragraph 2 ----	2,3,5,8
Y	WO 98 32333 A (MACKAY ALASTAIR M ; OSIRIS THERAPEUTICS INC (US); MURPHY J MARY (US) 30 July 1998 (1998-07-30) page 1, paragraph 1 -page 5, paragraph 2 page 10, paragraph 4 -page 12, paragraph 3; example 1; table 1 ----	2,3,5,8
Y	JOHNSTONE, B. ET AL.: "In vitro chondrogenesis of bone marrow-derived mesenchymal progenitor cells" EXPERIMENTAL CELL RESEARCH, vol. 238, no. 1, 10 January 1998 (1998-01-10), pages 265-272, XP000882426 the whole document ----	2,3,5,8
A	BORLAND, K. ET AL.: "Injectable Hydrogels Containing Autologous Chondrocytes as Engineered Tissue Bulking Agents" IN VITRO CELLULAR & DEVELOPMENTAL BIOLOGY ANIMAL, vol. 34, March 1998 (1998-03), page 28A XP000881997 the whole document ----	
A	HÄUSELMANN, H.J. ET AL.: "Adult human chondrocytes cultured in alginate form a matrix similar to native human articular cartilage" AMERICAN JOURNAL OF PHYSIOLOGY: CELL PHYSIOLOGY, vol. 271, no. 3, September 1996 (1996-09), pages C742-C752, XP000882049 cited in the application page C742, left-hand column, paragraph 1 -page C743, left-hand column, paragraph 3 ----- -/--	

INTERNATIONAL SEARCH REPORT

International Application No

T/US 99/27129

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>KUJAWA M J ET AL: "SUBSTRATE-BONDED HYALURONIC-ACID EXHIBITS A SIZE-DEPENDENT STIMULATION OF CHONDROGENIC DIFFERENTIATION OF STAGE 24 LIMB MESENCHYMAL CELLS IN CULTURE" DEVELOPMENTAL BIOLOGY 1986, vol. 114, no. 2, 1986, pages 519-528, XP000882647 ISSN: 0012-1606 the whole document -----</p>	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

T/US 99/27129

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9825653	A	18-06-1998	AU 5601598 A	03-07-1998
			AU 5698698 A	03-07-1998
			EP 0944403 A	29-09-1999
			WO 9825575 A	18-06-1998
			AU 9490898 A	12-04-1999
			WO 9915211 A	01-04-1999

WO 9628539	A	19-09-1996	US 5906934 A	25-05-1999
			AU 5251696 A	02-10-1996
			EP 0815203 A	07-01-1998
			ZA 9602020 A	24-10-1996

WO 9832333	A	30-07-1998	EP 0948255 A	13-10-1999

F I N T COOPERATION TREA

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
 United States Patent and Trademark
 Office
 Box PCT
 Washington, D.C.20231
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 31 August 2000 (31.08.00)	
International application No. PCT/US99/27129	Applicant's or agent's file reference 640100-352
International filing date (day/month/year) 16 November 1999 (16.11.99)	Priority date (day/month/year) 16 November 1998 (16.11.98)
Applicant KAVALKOVICH, Karl et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

15 June 2000 (15.06.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Claudio Borton Telephone No.: (41-22) 338.83.38
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PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C12N 5/06, A61K 35/28	A1	(11) International Publication Number: WO 00/29552 (43) International Publication Date: 25 May 2000 (25.05.00)
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(54) Title: ALGinate LAYER SYSTEM FOR CHONDROGENIC DIFFERENTIATION OF HUMAN MESENCHYMAL STEM CELLS (57) Abstract Disclosed are a composition of chemically defined components which support <i>in vitro</i> and <i>in vivo</i> chondrogenesis of mesenchymal stem cells, a method for <i>in vitro</i> and <i>in vivo</i> chondrogenic induction of such stem cells, and a method of forming human chondrocytes <i>in vitro</i> and <i>in vivo</i> from such stem cells.		

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